Certificate of Affidavit

State of Israel)
Tel Aviv/Yafo Municipality)
Embassy of the United States) SS:
of America)

I certify that on this day the individual named below appeared before me and, being sworn, made the statements set forth in the attached instrument.

Mrs. Liat Tsoref

X ____________________
(Signature of Consular Officer)

Lisa Bess Wishman

Consular Officer of the United States of America
commission does not expire

September 1, 2004

(SEAL)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	L. TSOREF et al.
Serial Number:	10/042,735
Filed:	October 25, 2001
For:	BONE AGE ASSESSMENT USING ULTRASOUND
Art Unit:	3737
Examiner:	JAWORSKI, FRANCIS J

Honorable Commissioner of Patents
P.O. Box 1450
Alexandria, VA 22313-1450

AFFIDAVIT UNDER 37 CFR 1.131

I, Liat Tsoref presently of 26 Anatot St., Tel Aviv, Israel, am an inventor of subject matter described and claimed in claims 1-63 of the US Patent Application identified above and hereby declare:

1. I reduced to practice the invention claimed in the above noted claims on a date on which I carried out experiments on children that indicated that through measurements of ultrasound at a location of their skeletal structure associated with bone growth during maturation are correlated with their ages. The experiments were carried out on two healthy children of different ages and measurements were acquired for each child at the ends of the radius and ulna bones near the hand.

The date on which the experiments were carried out, July 4, 2000, is prior to the filing date of US Patent Application Publication 2002/0162031.

2. Measurement data acquired from the children on the date of the experiments are shown in a photocopy, attached hereto as exhibit A, of a page from my log book in which I recorded the data. The date on which the data was acquired is indicated by the date shown

in the upper left hand corner of the log book page. English text in curly brackets with an arrow pointing to Hebrew text in the original document is added to explain the Hebrew text to which the arrow points.

Liat Tsoref

Liat Tsoref

Sworn to and subscribed before me

on this ____________________

____

Notary Public

4/7/00

Bone Age

300 kHz

{Date}

{Probe Position} מיקום	{Speed of sound m/s} מהירות	{Time} זמן	{Distance} מרחק	
[illegible]	2267	16.217	36.76	[illegible]
2.75 delay [illegible]	2730	13.47		
[illegible]	1640	32.75 − 2.75 = 30	49.20	יובל
" " "	1678	36.06 − 2.75 = 33.31	55.89	עמית
{Radius-Ulna} רדיוס - אולנה	1916	26.95 − 2.75 = 24.2	46.36	עמית
" " 300 mV	1725	29.06 − 2.75 = 26.31	45.38	יובל
" " 152 mV	1703	28.90 − 2.75 = 26.15	44.53	יובל
" " 32 mV	1925	26.46 − 2.75 = 23.71	45.65	עמית

{Child "Amit" 10 5/12 yr}

TOHSC Attenuation = 0

Amplification = 0

{Child "Yuval" 5 11/12 yr}

8ms [illegible]

1μs [illegible]

Exhibit A

ATTY DOCKET NO.	SERIAL NO.
082/02329	10/042,735
Liat TSOREF, et al.	
FILING October 25, 2001	GROUP 3737

INFORMATION DISCLOSURE CITATION

(Use several sheets if necessary)

U.S. PATENT DOCUMENTS

EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE

FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES	TRANSLATION NO

OTHER DOCUMENTS (Including Author, Title, Date, Pertinent Pages, Etc.)

		6	TODD, T. W.; "Age Changes in the Pubic Bone;" pp. 285-334; American Journal of Physical Anthropology; Vol. 3.; No. 3; July-September 1920
		7	TODD, T. W. et al.; "Endocranial Suture Closure, its Progress and Age Relationship;" American Journal of Physical Anthropology; Vol. 7; pp. 325-384; 1924

EXAMINER	DATE CONSIDERED
[signature]	3-4-04

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

OIPE JC110
SEP 1 0 2004
PATENT & TRADEMARK OFFICE

INFORMATION DISCLOSURE CITATION
(Use several sheets if necessary)

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October 25, 2001	3737

U.S. PATENT DOCUMENTS

*EXAMINER INITIAL		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
	1	6,280,402	28 AUG '01	ISHIBASHI, Y. et al.			

FOREIGN PATENT DOCUMENTS

		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES	TRANSLATION NO

OTHER DOCUMENTS *(Including Author, Title, Date, Pertinent Pages, Etc.)*

EXAMINER [signature] DATE CONSIDERED 3-4-04

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609; Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Form PTO-A820
(also form PTO-1449)

P09C/REV03

Patent and Trademark Office • U.S. DEPARTMENT OF COMMERCE

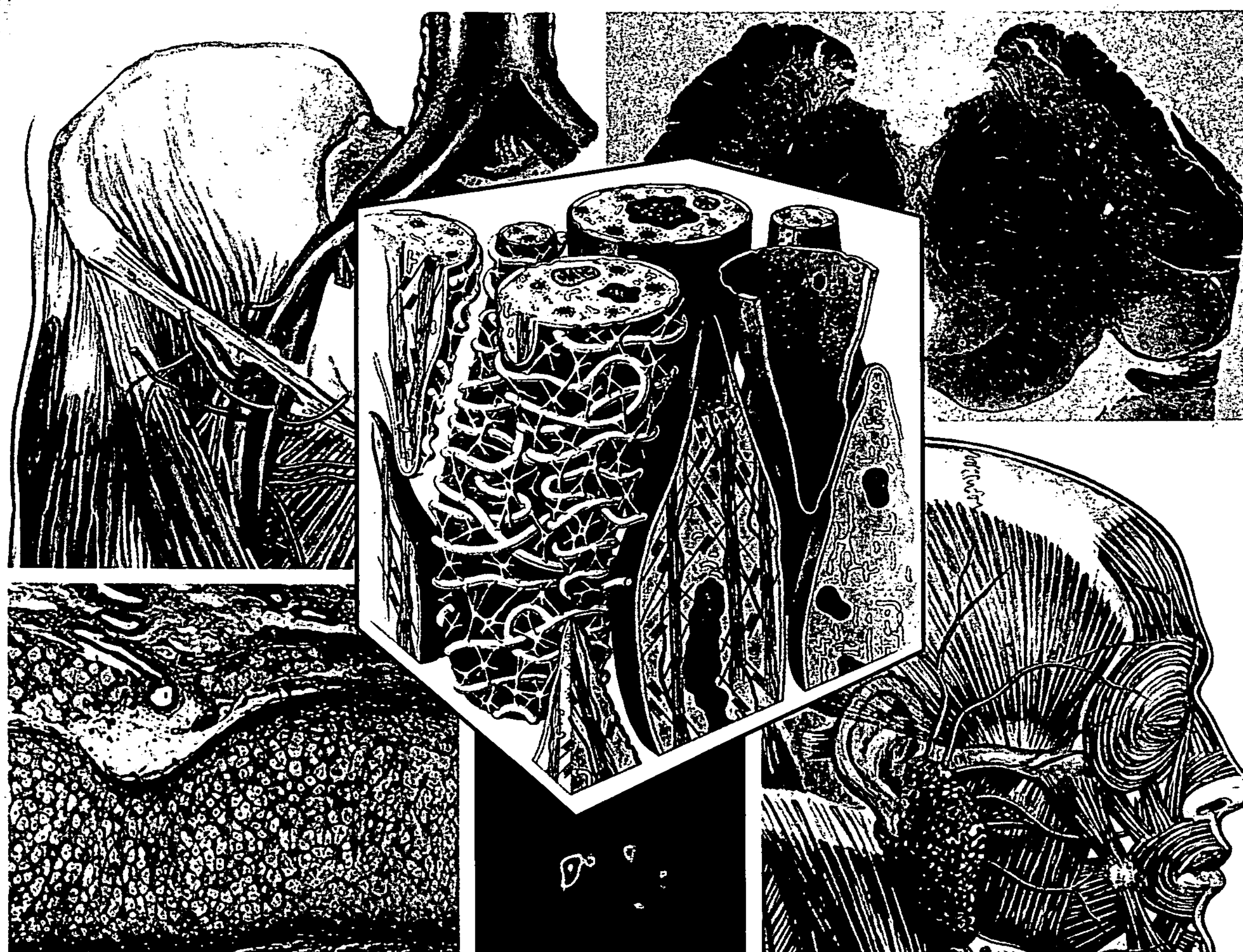
6

4

Henry Gray

THIRTY-EIGHTH EDITION

GRAY'S ANATOMY



CHURCHILL LIVINGSTONE

culture and transplantation of embryonic skeletal tissues (Murray & Huxley 1924; Fell & Canti 1934; Willis 1936); all major characteristics appear to be self-determined. Mechanical influences such as moulding by muscular activity, often regarded as of first importance, do not operate when the primary form is being established. As muscles become active during prenatal life they may influence bone growth, but to what extent is difficult to say; after birth and up to adolescence, before all the epiphyses are fused, increased activity augments growth in both length and girth. The reduced limb bone growth seen in paralyses, for example poliomyelitis, implies that muscle activity is necessary for proper skeletal development. Experimental studies involving removal of muscles point in the same direction (Appleton 1934; Washburn 1947; Wolffson 1950). Increases in strength and stature show some temporal correlation in adolescents (Jones 1949).

Metabolic influences affect bone growth at all stages of development. The availability of calcium, phosphorus, vitamins A, C and D, and secretions of the hypophysis, thyroid, parathyroid, adrenal glands and gonads, are all essential to osteogenesis (see below) and hence to skeletal form and dimensions. Disturbances in any of these factors result in recognized pathologies; however, it is often difficult to distinguish pathological from normal variation. Body height is an example: between the extremes of dwarfism and gigantism (both resulting from hormonal dysfunction), much variation in height occurs. Variations in stature and other dimensions linked with age, sex and race are in part genetically determined; but racial variations in nutrition also have profound effects (Greulich 1951; Acheson 1960; Tanner 1962).

Body proportions and absolute dimensions vary widely in respect of age and sex (**6.7**) within and between racial groups. While partly due to variability in muscularity and adiposity, such variations are chiefly skeletal; their study is *anthropometry* (Martin 1928: Hrdlička 1939). The data of anthropometry may be non-metrical, such as the presence or absence of a feature (e.g. sagittal crest in Eskimo skulls, preauricular sulcus in female innominate bones), or persistence of an entity (e.g. interfrontal suture), or degree of development (e.g. frontal ridges, projection of chin). However, most anthropometric data are measurements, by internationally agreed techniques, in living subjects or skeletal material. These may involve the whole body (e.g. stature), sections such as the limbs, or individual bones. Proportions are expressed by indices, for example breadth of the skull as a percentage of its length (the *cranial index*), which may show ethnic variation. Mongoloid people, for example, have larger cranial indices than other races; they therefore have a relatively 'broader' head, which is also absolutely wider. A Mongolian child, of course, might have a cranial width less than that of a Negro adult, and yet be proportionately broader. Ratios between length of limbs and 'sitting height', or between arm and leg, upper arm and forearm, thigh and foreleg, are all used and show differences related to age, sex and race. Details of some indices, where appropriate, are included in accounts of particular bones.

Observations and measurements suggesting age, sex, size and race of an individual skeleton, or parts of it, are not only useful in anthropology and archaeology (Brothwell 1968; Warwick 1968) but sometimes essential to identification in forensic practice (Glaister & Brash 1937; Boyd & Trevor 1953; Stewart 1954; Harrison 1957).

Estimation of skeletal age

Estimation of skeletal age involves many criteria, varying in value at different ages. Up to 25 years (including fetal life) dentition and ossification provide numerous data for assessment of age, with accuracy dependent on precision of observations, available statistics for sex and racial affinities of individuals under examination, together with their nutritional and endocrine history. The latter data are rarely forthcoming; available tables of ossification usually apply to healthy caucasian children and adolescents in Europe or America. A few studies of other racial groups exist (Todd 1931; Modi 1957): racial variations in the events of ossification would necessarily be genetic, but there is no clear evidence for this (Krogman 1962). Variations in ossification are affected by the wide divergence in nutrition between and within racial groups so far studied, in all of which data females show earlier ossification and epiphyseal fusion than males, a difference which is presumably genetic. Nevertheless, up to age 25, the age of a complete skeleton can usually be assessed to within a year, or more accurately in earlier years, especially if dental observations are available. (For details see Teeth and individual bones.)

Above 25 years skeletal age can be estimated to within five years by the appearance of the cranial sutures and of the bony surfaces of the symphysis pubis. From midtwenties onwards, sutures exhibit progressive closure (p. 607, Todd & Lyon 1924, 1925a, b, c), which begins internally, so that without internal inspection observations may be misleading (Singer 1953; Genovese & Messmacher 1959); complications due to racial variation have been recorded (Abbie 1950). Progressive changes occur in the articular surfaces at the pubic symphysis. Features typical of ages from late teens to fifties and beyond are well-established (Todd 1920a, b, 21a, b; McKern & Stewart 1957), and this is generally considered the best method for estimation of skeletal age in maturity. Sequences of age changes have also been described in other bones (scapula, sternum and costal cartilages), but provide less accurate estimates. Lipping of the rims of vertebral bodies and at other articular surface margins, exaggerated secondary markings and ossification into tendons and ligaments all suggest advancing age, but only vaguely indicate **actual** age.

Estimation of sex

Estimation of sex in complete postpubertal human skeletons is usually easy, even without measurement. Sexual differences are marked in the pelvis (p. 673) and skull (p. 609), but not equally so in all populations. Thus 'sexing' of skeletons from one racial group is almost free from error, whereas assessment of an individual of unknown extraction is less certain. Postcranial bones other than the pelvis, especially larger limb bones, may provide clear evidence of sex, if others of like race and both sexes are available for comparison. Female bones are usually smaller and more slender than male equivalents, i.e. smaller shaft diameter relative to length. This is reflected in their comparative **weights**: in a study of Hindu femora, mean weights were 385 g in males, 279 g in females (Singh & Singh 1974).

Anatomists, anthropologists, and forensic scientists have long judged the sex of skeletal material by non-metrical observations. More recently, sexual divergence has been based upon measurements in many different bones (Montagu 1960; Krogman 1962). Discriminant analysis, for example, in which the capital dimensions of 70 humeri were analysed (Rother et al 1977), showed that sex was not easy to establish; however, approximate age could be assessed. Such studies emphasize the need for standards of sexual dimorphism in different populations. The pelvis remains, however, the most reliable region for assessing sex even before puberty, as well as in infancy (Reynolds 1947) and fetal life (Boucher 1957).

Sexual dimorphism of thoracolumbar vertebrae in Australian subjects (aged 5 to 19 years) has been observed by Taylor and Twomey (1984), with female vertebral bodies being more slender from the eighth year onwards: there being greater growth in transverse diameter in males.

Estimation of size

Estimation of size, particularly height, from measurements of limb bones has long been formulated (Rollet 1899), and with increasing accuracy as formulae have become more refined (Trotter & Gleser 1958). All such calculations depend on the fact, familiar to artists (cf. Leonardo da Vinci), that major parts, trunk and limbs, exhibit consistent ratios among themselves and relative to total height; these ratios are linked to age, sex and race. The relatively large head, long trunk, short arms and shorter legs present a familiar picture in infants which becomes grotesque in older children, and monstrous in adults. As infants grow, they change their proportions gradually towards adult shape, diverging towards one sex at puberty. The limbs become relatively longer, the shoulders broader and the pelvis narrower in adult males, as well as other differences (**6.7**). Between major races, and even smaller ethnic groups, characteristic variations in proportions appear. Negroes have comparatively long legs and arms: moreover, the calf and forearm are long relative to the thigh and arm. Consequently, formulae designed to estimate height from long bones in one population may not apply to another. Alternative formulae for the sexes must also be used, and immature bones must be recognized and suitable corrections made.

Femoral length alone has commonly been used for estimating stature by using a simple multiplier derived from comparison with